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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,927	08/17/2001	Glaucia Paranhos-Baccala	110048	1582

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Oliff & Berridge
PO Box 19928
Alexandria, VA 22320

EXAMINER	
CHAKRABARTI, ARUN K	

ART UNIT	PAPER NUMBER
1634	8

DATE MAILED: 02/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/869,927	Paranhos-Baccala
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 17, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-31* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *09/869,927*.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-11, 16, 19-21, and 24-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for multiple sclerosis does not reasonably provide enablement for any possible autoimmune disease or unsuccessful pregnancy or pathological conditions of pregnancy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Court in re Wands, 8 USPQ2d 1400 (CA FC 1988) stated with regard to enablement that

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

Here, the claim is broadly drawn to any autoimmune disease or unsuccessful pregnancy or

pathological conditions of pregnancy, which meets the criteria of the use of portion of the gag gene. However, the specification does not provide guidance commensurate in scope with this claim, teaching only multiple sclerosis which meets the requirement. The specification provides minimal guidance regarding methods for the isolation of additional nucleic acid fragments which meet this autoimmune disease or unsuccessful pregnancy or pathological conditions of pregnancy requirement. The specification also provides one working examples, which are represented by the detection and treatment of multiple sclerosis. The cited prior art of FR-A-2 765 588 (BIO MERIEUX, January 8, 1999) shows that in a screening assay, only serum of MS patients were recognized (page 29, line 8 to page 30, line 21 and the table, page 29). This demonstrates the unpredictability of the event, since BIO MERIEUX was testing gag gene with active site mutations, and found only a single disease with the desired function. While the skill level in the art is high, it is therefore highly unpredictable whether other autoimmune diseases can be identified which meets this specific criteria regarding the use of portion of the gag gene. Further, identification of additional mutations will be by the trial and error method. This trial and error requirement is borne out because protein structural effects caused by mutations cannot be readily deduced, even where the crystallographic structures are known. Further, each mutation has unpredictable effects on protein function, and no general method for a priori selection of functional mutations is presented. It would require a large amount of experimentation, potentially including the synthesis of hundreds of mutations, in order to identify additional autoimmune diseases with the claimed functionality. Given the Wand's factors opposing the full scope of

enablement including the limited teaching in the specification, the presence of only one working example, the teaching of unpredictability in the prior art, the unpredictability of the art, the breadth of the claim, and the large amount of experimentation needed, with only the skill level in the art supporting enablement, it is concluded that undue experimentation is necessary to make and use the invention as broadly claimed.

3. Claims 1-12, 16, and 19-31 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In Example 2 of the specification, reference is made to a 2009 bp nucleotide sequence (SEQ ID NO: 2) coding for the polypeptide described in SEQ ID NO: 1. However, it is not at all clear how the sequence is obtained since neither of the two 5' primers described in Example 2 can be found in the sequence.

Moreover, there is no evidence in the specification of the application that transcription/translation products, as obtained according to the method of claim 11, or synthetic peptides from SEQ ID NO: 31 can be used in the study and/or monitoring of in vitro T cell proliferation. Therefore, the subject matter of claim 12 and any claim related to SEQ ID NO: 31 are not supported by the written description of the present application.

4. Claims 1-7, 16, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is rejected over the recitation of the negative limitations " but not belonging to SEQ ID NO: 1." (See MPEP 2173.05 (I)) -- "Any negative limitation or exclusionary proviso must have basis in the original disclosure. See *Ex parte Grasselli,* USPQ 393 (Bd. App. 1983), *aff'd mem.,* 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement". In the instant application, negative limitations inserted in the amended claims do not have any expressed basis in the original specification.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 8-11, 13, 19-21, 26, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 8 and 10, the phrases "for instance", and "in particular" render the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claim 8, the phrases "capable of" and "preferably" render the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention.

Claim 13 is rejected over the recitation of the phrase, "part of SEQ ID # 3". In absence of a definition of the part of the sequence, the metes and bound of the claim is vague and unclear because a single nucleotide is also a part of the SEQ ID# 3, which certainly cannot be used in situ molecular labeling of chromosome as claimed.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-11, 13-16, and 19-31 are rejected under 35 U.S.C. 103 (a) over European Patent Publication FR-A-2 765 588 (BIO MERIEUX) (January 8, 1999).

FR-A-2 765 588 (BIO MERIEUX) relates to nucleic material, optionally consisting of a retroviral material, in an isolated or purified state (page 5, lines 26-29). Example 5 of FR-A-2 765 588 (BIO MERIEUX) also describes, in particular, the production of the CL2 clone containing a part homologous to the pol gene (corresponding to the protease gene) and to the gag gene (GM3) (corresponding to nucleocapsid) in 3' and a new 5' coding region corresponding to the gag gene and, more specifically, to the MSRV-1 matrix and capsid (page 25, lines 10-15). The protocol used for identifying and isolating the clone (page 25-27) is exactly the same as the one described in Example 1 of the present application (including the nucleotide primers used for the PCR) and also leads to isolation of the 1511 bp sequence described in SEQ ID NO: 1 of the present application (page 27, line 22 and page 42, SEQ ID NO: 130). This sequence has a 1056 bp open reading frame coding for a 352 amino acid protein (Figure 6: 13/27 to 16/27: second open reading frame). D1 indicates that the sequence corresponding to the open reading frame has been cloned into two expression vectors pET28C and pET21C (page 28, lines 9-12). Finally D1 describes the expression of the CL2 clone in Escherichia coli (Example 6: pages 28-30) and discloses that the polypeptide expressed by both clones is indeed recognized by the serum of multiple sclerosis patients (page 29, line 8 to page 30, line 21 and Table, page 29). This work is the same as that illustrated in Example 3 of the present application (pages 22-23).

Moreover, FR-A-2 765 588 (BIO MERIEUX) claims a diagnostic, prophylactic or therapeutic compositions containing, inter alia, the sequence described in SEQ ID NO: 130 or the complementary sequence thereof (page 9, lines 1-5) as well as a method for detecting a retrovirus associated with multiple sclerosis using the sequences (page 9, lines 6-12).

FR-A-2 765 588 (BIO MERIEUX) also indicates that, in the case of MSRV-1, there are endogenous retroviral sequences in human DNA that include sequences homologous to the MSRV-1 genome (page 2, line 30 to page 3, line 6) as well as that these endogenous retroviral elements can be important (page 3, lines 1-25).

An ordinary artisan who knows the nucleotide sequence of the MSRV-1 "exogenous" retrovirus gag gene from FR-A-2 765 588 (BIO MERIEUX) and is aware that the sequence has an open reading frame coding for a 352 amino acid protein recognized by the serum of multiple sclerosis patients, and that human DNA contains endogenous retroviral sequences homologous to the MRSV-1 genome, would not have had to exercise any inventive skill to consider isolating sequences corresponding to the MRSV-1 gag gene in the human genome by means of techniques that are well known to a person skilled in the art, and to envisage using the sequences or the proteins encoded thereby in multiple sclerosis diagnosis or therapy.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703)

306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

January 23, 2003

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600